

**REMARKS**

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-49 are in this case. Claims 36-49 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-35 have been rejected. Claims 3-5, 12-14, 21-23, 30-32 and 36-49 have been canceled. Claims 36-49 drawn to a non-elected invention have been canceled, but Applicant reserves the right to file a divisional application thereon at a later date. Claims 1-2, 6-11, 15-20, 24-29 and 33-49 have been rejected. Claims 1, 9, 18 and 27 have now been amended.

***Claim Objections***

The Examiner has objected to claim 9 because the phrase "fuse to" is mistakenly repeated twice. Claim 9 has now been amended to remove the repetition.

***35 U.S.C. § 112, First Paragraph, Rejections***

The Examiner has rejected claims 1-2, 6-11, 15-20, 24-29 and 33-35 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention. The Examiner's rejections are respectfully traversed. Claims 1, 9, 18 and 27 have now been amended.

The examiner points out that no support is found in the specification for the phrases "separately expressed" and "a Ras activity".

With respect to the phrase "separately expressed" claims 1, 9, 18 and 27 have now been amended such that the term "separately" has been removed from the phrase "separately expressing" to thereby overcome the Examiner's rejections to these claims under 35 U.S.C. § 112, first paragraph.

With respect to the phrase "a Ras activity" Applicant wishes to point out that currently amended claims 1, 9, 18 and 27 recite a cell (or cells) "lacking Ras activity" and "detecting Ras activity in said cell (or cells). Accordingly, Applicant wishes to

direct the Examiner's attention to page 23 lines 12-18 of the instant application which recites the following:

"The cell lacking Ras activity described herein can be any cell including mammalian and insect cells which can be Ras mutated provided restoration of Ras activity produces a detectable signal or change in a phenotype. Preferably, the cell is a Cdc25-2 yeast cell which is incapable of growth under restrictive conditions characterized by a temperature in the range of 32-40 °C. In such cells translocation of the cytoplasmic Ras mutant to the plasmalemma enables growth under such restrictive conditions."

Applicant further wishes to direct the Examiner's attention to Figure 3 of the instant application illustrating a preferred procedure for detecting Ras activity in cells (based on cells capacity to grow at restrictive temperature range).

Hence, it is the Applicant's strong opinion that the instant application adequately describes a cell lacking Ras activity and for detecting Ras activity (and the lack of) in a cell in a way which reasonably conveys an ordinary person skilled in the art how to make and use the invention.

In view of the above arguments, Applicant believes to have overcome the 35 U.S.C. § 112, first paragraph, rejections.

### ***35 U.S.C. § 112, Second Paragraph, Rejections***

The Examiner has rejected claims 1-2, 6-11, 15-20, 24-29 and 33-35 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiners rejections are respectfully traversed. Claims 1, 9, 18 and 27 have now been amended.

The Examiner points out that the metes and bounds of the phrases "separately expressing" and "absence of expression of said first polypeptide" are unclear.

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Claims 1, 9, 18 and 27 have now been amended such that the phrase "separately expressing" has been deleted from the claims to thereby overcome the Examiner's rejections under 35 U.S.C. § 112, second paragraph.

### ***Double Patenting***

The Examiner has provisionally rejected claims 1 and 6 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1 and 3-4 of opening U.S. Pat. Application No. 09/765,298 (hereinafter 09/765,298). The Examiner's rejections are respectfully traversed. Claims 1 and 6 have now been amended.

The Examiner points out that claims 1 and 3-4 of U.S. Patent Application No. 09/765,298, now U.S. Pat. No. 6,582,927, anticipate claims 1 and 6 of the instant application. A Terminal Disclaimer in compliance with 37 CFR 1.321 to overcome the double patenting rejection has been filed and accepted.

### ***35 U.S.C. § 102(a) Rejections***

The Examiner has rejected claims 1, 6-8, 18-19 and 24-26 under 35 U.S.C. § 102(a) as being anticipated by Takemaru and Moon, The Journal of Cell Biology 149(2), April 17, 2000. The Examiner's rejections are respectfully traversed. Claims 1, 9, 18 and 27 have now been amended.

The Examiner points out that Takemaru and Moon teach expression of pRas(61) $\Delta$ F- $\beta$ catR8-C which is comprised of the activated c-HaRas mutant and  $\beta$ -catenin in the cdc-2 yeast strain. Library cDNAs are fused to the v-Src myristoylation sequence targeted to the plasmalemma to identify polypeptides that interact with pRas(61) $\Delta$ F- $\beta$ catR8-C as characterized by Ras activity. The Examiner asserts that it is not clear how the limitation of separately expressing the first and second polynucleotides distinguishes the present invention from Takemaru and Moon. In addition, the Examiner asserts that it is inherent in the teachings of Takemaru and Moon that the cells are transfected in the presence and absence of the first polynucleotide.

In an earlier response dated 6/1/04 (filed 6/3/04) Applicant argued that identifying interactions between polypeptides using the method according to the

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claimed invention is distinct and substantially advantageous over prior art methods which do not employ the unique false positive eliminating step of the present invention. Specifically, these limitations relate to a feature of the method of the present invention which enables to discount Ras membrane translocation which does not result from an interaction between the tested polypeptides. Such a feature is neither described nor suggested by Takemaru and Moon and as such, by employing this unique false positive eliminating step (i.e., detecting Ras activity only in cell(s) grown under predetermined conditions which are selectively inductive for expression of the first polypeptide), the present method is vastly superior to the method described by the reference method. For example, a cytoplasmic Ras mutant fused to a membrane protein can often result in membrane mobilization of Ras which is independent of interaction with the expressed "bait" polypeptide (see page 26 lines 7-11 of the instant application). Consequently, the need to reduce incidence of such false positive errors inevitably requires performing additional laborious, time consuming and costly controls and repeat assays.

In order to overcome the Examiner's rejections claims 1, 9, 18 and 27 have now been amended such that the term of "separately" (expressing the first and second polynucleotides) and the phrase "in the presence and absence of" (expression of said first polypeptide) have been deleted. In addition, the amended claims now recites that the first polynucleotide (encoding a first polypeptide being capable of interacting with a plasmalemma of the cell) is "operably linked to an inducible promoter" and that detection of Ras activity is effected when cells are grown only under "inductive conditions which result in expression of said first polypeptide from said inducible promoter".

Thus, in contrast to the referenced method, the present invention includes a step of positively determining expression of a first polypeptide (capable of interacting with the plasmalemma) in a cell. This step can be effected by expressing in a cell lacking Ras activity (as defined on page 23 lines 12-18 of the instant application) the first polynucleotide and the second polynucleotide, whereas the first polynucleotide is positioned under the transcriptional control of an inducible promoter. Determining the presence of the first polypeptide expression is effected by culturing the transformed cell under predetermined inductive or

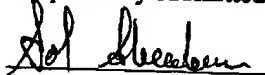
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suppressive conditions (e.g., presence or absence of inducing or suppressing agents in the culture medium; see in Example 1 and Figures 3-5 of the instant application). Thus, according to the teachings of the present invention as recited in currently amended claims 1, 9, 18 and 27, only an expression of the first polypeptide which coincides with Ras activity (e.g., capacity to grow at high temperature) would be considered as a positive identification of an interaction between the tested polypeptides. In sharp contrast, the teachings of Takemaru and Moon do not describe or suggest any step of distinguishing between cells exhibiting Ras activity which results from expression of the target polypeptide and a Ras activity which results from mobilization of Ras to a non-target plasmalemma polypeptide (i.e., false positive).

In view of the above described amendments and arguments presented it is Applicant's strong opinion that claims 1, 6-8, 18-19 and 24-26 are neither anticipated nor rendered obvious by the teachings of Takemaru and Moon.

In view of the above amendments and remarks it is respectfully submitted that claims 1-2, 6-11, 15-20, 24-29 and 33-35 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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**Encl.:**

Request for Continued Examination  
Extension of time fee.